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SERIAL NUMBER	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
07/460,878	02/02/90	EKINS R	

EXAMINER	
WOODWARD, M	

ART UNIT	PAPER NUMBER
1813	6

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DATE MAILED: 01/27/92

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☒ Responsive to communication filed on NOV 4, 1991 ☒ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), ___ days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☐ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice re Patent Drawing, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, Form PTO-152
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☒ Claims 1-11 are pending in the application.
   Of the above, claims _____ are withdrawn from consideration.
2. ☐ Claims _____ have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 1-11 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).
12. ☒ Acknowledgement is made of the claim for priority under U.S.C. 119. The certified copy has ☒ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____.
13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1813.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The specification is again objected to under 35 U.S.C. § 112, first paragraph, as failing to adequately teach how to make and/or use the invention, i.e. failing to provide an enabling disclosure.

Claims 1-11 are again rejected under 35 U.S.C. § 103 as being unpatentable over applicant's own admissions of the prior art.

Applicant's arguments filed November 4, 1991 have been fully considered but they are not deemed to be persuasive. In light of Applicant's arguments the rejections made under 35 USC §112, second paragraph are withdrawn. The Examiner also withdraws the previous objection to applicant's attempt to incorporate material by reference.

35 USC §112, FIRST PARAGRAPH

The Examiner withdraws that portion of the objection concerning the teachings on insignificance.

In the prior office action the Examiner stated

> Applicant then argues that employing low levels of antibody such that the concentration of antigen is effectively unchanged by antigen bound to antibody is "contrary to generally recommended practice in the field of immunoassay." This argument is misleading. It is true that a segment of the workers in the field of immunoassay have developed a particular standardized fashion for measurement;

> applicant has played a significant role in this area, even as late as 1985 (Dudley et al.). The teaching of the art is that the apparently optimal conditions for a sensitive, reliable immunoassay are those in which approximately 50 percent of the tracer is bound. This is not a teaching that other methods will not work.

Applicant has responded by stating that a factual basis for the statements made in the specification exists and that it was not intended to be misleading. In response the Examiner argues that while applicant may have presented factual information it was only that which permitted the construction of a strawman. Applicant is atempting to positively bias the reader's view of the nonobviousness and novelty of the instant invention by calling attention to a particular species of immunoassays rather than viewing the entire genus. The ordinary artisan with an understanding of binding equilibria recognizes that the equation on page 2 is accurate only when the total ligand concentration is effectively unchanged by the presence of bound ligand.

35 USC §103

In the prior office action the Examiner made the following rejection

> On page 1 of the specification applicant states that in WO84/01031 he proposed making quantitative measurements of analytes using trace amounts of specific antibodies and on page 3 it is disclosed that UK Patent Application 2,099,578A concerns a device for analysing a plurality of specimens. A similar device is disclosed in Chang (US Patent 4,591,570). It would have been obvious to a person of ordinary skill in the art at the time the invention was made to simultaneously quantify several analytes using trace levels of antibody in a device such as that described by Chang because it would be expected to work.

Applicant has responded with two lines of argument. In the first applicant argues that

> "many experienced immunologists, when first introduced to the methodology of the present invention cannot immediately understand why it is that amounts of analyte vastly in excess of the amount of antibody in the system do not result in total occupancy of all antibody binding sites."

and that the instant invention

> (a) it uses far less antibody than is conventional (...),
> (b) its sensitivity is at least equal to, and in principle greater than, that obtainable using conventional assays, and
> (c) that this high sensitivity can be acheived using incubation times that are as short, and, in principle, shorter than other conventional approaches.

Applicant argues that advantages (b) and (c) are unexpected and provides a figure as support.

The Examiner does not find the first argument persuasive since it will depend on how the invention is presented and whether or not the particular immunologist is concerned with developing immunoassays.

The Examiner finds that there is an inadequate explanation of how the data were generated in the figure. It would appear as if the curves are plotted using the total analyte concentration which in the case of significant bound analyte is inappropriate. The graph for low antibody concentration is effectively looking at the fraction bound at a given free analyte concentration whereas that at high antibody conentration is looking at total analyte concentration when it should be viwed in terms of free analyte. In looking at the curves it appears that when more antibody is present that equilibrium is reached sooner which is the exact opposite of point (c).

Applicant's second line of argument is that the Examiner has not presented a prima facie case of obviousness. It appears that

applicant believes that the knowledge of the amount of antibody to immobilize so that the amount of analyte bound is insignificant compared to the total analyte concentration is not apparent to one of ordinary skill in the art from examining the binding equation on page 2 of the specification. Given the affinity constant of the antibody, the range of analyte concentrations of interest, and the assay volume one can calculate the maximum amount of antibody which can be present so that an insignificant amount of analyte will be bound compared to the total analyte concentration. Having made such calculations one of ordinary skill in the art would proceed to apply the antibodies to the devices known in the prior art.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a). The practice of automatically extending the shortened statutory period an additional month upon the filing of a timely first response to a final rejection has been discontinued by the Office. See 1021 TMOG 35.

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Woodward whose telephone number is (703) 308-3890.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Group 180 by facsimile transmisssion. Papers should be faxed to Group 180 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

The CM1 Fax Center number is (703) 308-4227.

CHRISTINE NUCKER
PRIMARY EXAMINER
ART UNIT 1813

MP Woodward
January 23, 1992